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Please send me:
1. Donnelly, J.J., Ulmer, J.B., Liu, M.A. Minireview: DNA vaccines. Life Sciences vol. 6 no. 3, pp 163-172 (1997)

2. Ulmer, J.B., Sadoff, J.C., and Liu, M.A. DNA vaccines. Current Opinion in Immunology vol. 8, no. 4, pp 531-536 (1996)

3. Donnelly, J.J., Ulmer, J.B., and Liu, M.A. Immunization with DNA. Journal of Immunological Methods vol. 176 no.2, pp 145-152 (1994)

4. Thomas, L.J., Pickard, M.D., Stewart, S.E., Waite, B.C.D., Lin, A.Y., Rittershaus, C.W., Pettey, C.L. A plasmid-based vaccine to elicit autoantibodies to cholesteryl ester transfer protein (CETP) for the prevention/treatment of atherosclerosis. Journal of Allergy and Clinical Immunology 99 (1 part 2):pS187 (1997)

5. Kyoo, Jang Moon, Byung-Yoon, Ahn, Tae-Lin, Huh, Song-Hae, Bok, Bok, Park Yong, Expression of cholesteryl ester transfer protein cDNA using recombinant vaccinia viruses. Journal of Biochemistry and Molecular Biology vol 28 no. 3, pp216-200 (1995).

Thank you.

Pick up 01/24/97

RC583.J6

754 **A Plasmid-based Vaccine to Elicit Autoantibodies to Cholesteryl Ester Transfer Protein (CETP) for the Prevention/Treatment of Atherosclerosis.** *LJ Thomas, MD Picard, SE Stewart, BCD Waite, AY Lin, CW Rittershaus, and CL Pettey.* T Cell Sciences, Inc., Needham, MA.

A plasmid-based vaccine was created which consisted of a nucleotide sequence encoding two regions of rabbit cholesteryl ester transfer protein (CETP) linked to a sequence encoding a tetanus toxoid fragment, in a vector where expression was driven by the CMV promoter/enhancer. This vaccine was designed to induce the production of autoantibodies to CETP, a key element of cholesterol and triglyceride transport. We believe these autoantibodies will inhibit CETP activity, prevent the transfer of cholesterol from HDL to LDL, and could prevent/treat atherosclerosis.

Rabbits which were vaccinated intramuscularly with this plasmid-based vaccine showed a decrease in serum cholesterol after vaccination. Rabbits were put on a high cholesterol diet to induce the formation of atherosclerotic-like lesions. Vaccinated rabbits which produced antibodies to CETP had overall lesser aortic lesions, as compared to unvaccinated animals. Similar vaccines could possibly be used in humans to offer long-lasting prevention or treatment of atherosclerosis.

755 **Reversal of Doxorubicin-induced Myelosuppression by CP-64131 in Dogs.** *D.W. Mann, N.A. Cusack, C.F. Petras, and E.J. Natoli* Pfizer Central Research Division, Groton, CT 06384.

CP-64131 is a novel immune stimulant with a variety of immunomodulatory activities. The compound is a 230 molecular weight 2-aminobenzazapine derivative. Its immune stimulant properties were initially discovered in an empirical rat macrophage based CSF inducer/agonist screen. It has direct proliferative effects in vitro on murine, bovine, porcine, and canine bone marrow. The bovine bone marrow proliferative activity is similar to the proliferative effects seen with bGM-CSF. The compound has also been shown to have direct effects in upregulating the cell surface expression of the adhesion molecule CD11b in both bovine and human PMN's, and primes human neutrophils for fMLP triggered oxidative burst activity. When administered in vivo to calves or dogs by intravenous, intramuscular, subcutaneous or most significantly an oral route, the compound induces dose dependent increases in serum G-CSF like activity, followed by a greater than 2 fold increase in numbers of circulating PMN's 24 hrs post administration. G-CSF has been used extensively as a therapeutic agent to reverse the myelosuppression following cytoreductive chemotherapy in cancer patients. We therefore tested whether CP-64131 induction of G-CSF like activity would have similar effects in reversing Doxorubicin induced myelosuppression in dogs. Treatment groups consisted of three dogs/group with Doxorubicin given at 1.5 mg/kg IV on day one, while Flunixin (NSAID) at 3.0 mg/kg IM and CP-64131 at 3.0 mg/kg SQ were given on days three and seven. The results of two studies indicate that administration of CP-64131 did reduce the extent and duration of the myelosuppression after Doxorubicin administration. We believe this is proof of the concept that a compound such as CP-64131 which induces CSF production in vivo can effectively reverse the myelosuppression that occurs following cytoreductive chemotherapy.

756 **Effect of Various Doses of Hydroxychloroquine on Circulating Adhesion Molecule ICAM-1 in Rheumatoid Arthritis (RA).** *KE Welch, RR Rothlein, E Mainolfi, DD Smith, and HB Lindsley.* University of Kansas Medical Center, Kansas City, KS and Boehringer Ingelheim, Ridgefield, CT.

As part of a large multicenter trial for the treatment of active RA, serum levels of soluble ICAM-1 were measured at study entry, week 6 and week 24. Levels were measured in 194 subjects by solid phase enzyme immunoassay. There were 3 groups of patients receiving hydroxychloroquine at doses of 1200 mg (Group 1), 800 mg (Group 2) or 400 mg (Group 3) per day for 6 weeks, with all 3 groups continuing at 400 mg daily until study completion. The mean (±SE) level of ICAM-1 in all patients was 423 (± 13) ng/ml. The mean level of ICAM-1 decreased by 15.4% in Group 1, 7.4% in Group 2 and 8.6% in Group 3. 80 of the 194 patients were found to have an initial elevated serum ICAM-1 level (> 450 ng/ml) with a mean level of 590 ng/ml. In this subset, the mean level of ICAM-1 decreased by 24.2% in Group 1, 21.6% in Group 2 and 21.9% in Group 3. The largest decrease occurred between entry and week 6 compared with week 6 to week 24. Even though only 41% of patients had elevated serum ICAM-1 levels, there was a downward trend in levels for all patients. The decrease was most marked in the subset of patients with levels > 450 ng/ml and in Group 1 with the highest initial dose of hydroxychloroquine. (Supported, in part, by Sanofi Winthrop, New York, NY)

757 **Restrictive TCRBV8S2 usage in the cochlear ear lesion of EAE mice.** *Kyung Mo [illegible] Kuang Chuan Cheng, Nacksung Kim, and Tai June Yoo* Univ. of Tennessee, Memphis, TN.

It has been reported that dominant expression of TCRVB8S2 gene segment in the EAE mice. In the previous study, we observed hearing loss in these EAE mice and a TCRBV8 monoclonal antibody prevented this central nerve disease as well as hearing loss. In this study, we focused the usage of TCRBV8S2 gene segment in the cochlear ear lesion of the EAE mice. The cochlear lesion was removed from EAE B10.PL mice at the clinical score 3, following the preparation of mPNA and cDNA. The results suggest that TCRBV8S2 gene only recombine to TCRBJ2S1 and TCRBJ2S7 gene segments. Both TCRBJ2S1 and TCRBJ2S7 gene segments have been identified in the EAE mice. Only the TCRBD2S1 has been observed in these TCR sequence. A enriched G, C insertion at the N regions between the V-D and D-J. More strictly, the results indicate that a length of 6 amino acids at the diversity region of these TCR sequence. These results suggest that a small subset of antigen specific TCR migrated and expanded at the cochlear lesion which leads to hearing loss.